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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,204	01/04/2001	Xiangzhong Yang	883933.0053	4830

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/755,204	Applicant(s) YANG ET AL.	
	Examiner Deborah Crouch	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 48-81 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 48-81 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 48-81 are pending.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 53, 54, 56, 57, 65, 67, 68, 71, 73, 74, 77, 79 and 80 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to embodiments encompassing humans. It is Patent Office policy not to allow claims that are drawn to or encompass humans (humans (1077 O.G. 24 April 21, 1987). Applicant can overcome this rejection by the insertion of the term "non-human" before animal, embryo and fetus.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48, 52, 59-64, 70, and 76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of cloning an animal and methods of forming a blastocysts where the donor nucleus, recipient oocyte and recipient animal are of the same species, does not reasonably provide enablement for these methods where the donor nucleus and recipient oocyte are of different species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass the transfer of a nucleus of a cell from one species of animal into the oocyte of another species, and/or where the foster mother is of a different species than the donor cell. However at the time of filing the art taught that such intra-species

combinations did not give rise to live births in predictable fashion. For example, in the production of sheep-goat chimeras, a high incidence of spontaneous abortion was observed, and explained by an incompatibility between the sheep recipient and the goat component of the conceptus (Fehilly, page 636, col. 2, parag. 2, lines 7-12). The specification provides no guidance for preventing fetal loss when the recipient female, oocyte and donor cell are all of distinct species.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50 and 52 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 52 lacks antecedent bases to claim 50. Claim 50 does not have language to "subpopulation."

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 48, 49, 51, 52, 59-61 and 70 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cibelli et al (1997) Science 280, 1256-1258.

Cibelli teaches the production of transgenic, cloned calves by the production of a bovine fibroblast cells from male fetal tissue, introducing a DNA sequence of interest operably linked to a promoter into the fibroblast cells, and performing nuclear transfer using

the transgenic fibroblast cell nucleus as the nuclear donor (page 1256, col. 3, parag. 1, lines 1-14). The nuclear transfer unit is activated and cultured to greater than a 2-cell embryo before transferring into a foster mother (page 1258, col. 2, note 12 to col. 3, line 12). The transferred embryo develops into a fetus, which develops into a term male calf (page 1257, figure 2). Fetal fibroblasts meant the definition of NENS somatic cells as they are neither embryonic nor sexual tissues. The production of live calves indicates that the doubling of the fibroblasts was sufficient to permit the introduction of the DNA sequence. 6.5 day embryos contain more cells than two. The introduction of the DNA sequence into the fibroblast cells is controlled as the procedure is regulated merely by the introduction of the DNA into the fibroblast cells. Therefore, Cibelli clearly anticipates the claimed invention.

Claims 53-58, 71-75 and 77-81 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cibelli et al (1997) Science 280, 1256-1258.

Cibelli teaches transgenic bovine embryos, bovine fetuses and live born calves produced by nuclear transfer (page 1257, figure 2). Organs are inherent to the fetuses and calves. Cibelli further teaches a cell line produced from the cloned transgenic calves (page 1257, figure 5). Thus Cibelli clearly anticipates the claimed invention.

Claim 63 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Presicce et al (1994) Molec. Reproduc. Develop. 37, 61-68.

Presicce teaches a method of nuclear transfer comprising activating the nuclear transfer embryo by incubation in media comprising ethanol and cycloheximide, followed by electro-stimulation (page 62, col. 1, parag. 3, line 6 to col. 2, line 3). Thus, Presicce clearly anticipates the claimed invention.

Claims 65-69 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Plump et al (1992) Cell 711, 343-353.

Plump teaches transgenic mice and transgenic mouse embryos whose genome comprises a disruption of in an apo-E gene such that functional apo-E is not produced (page 343, abstract). As the implanted transgenic mice embryos developed into transgenic mice, the intermediate of transgenic mouse embryos comprising the disruption is inherent to Plump. Organs and tissues obtained from the mice are also inherent to Plump (page 344, col. 1, parag. 1, lines 1-9). Further, in the process of producing the mice, Plump teaches and embryonic stem cell line that comprises the same apo-E gene disruption as the mice of Plump (page 343, col. 2, parag. 2, line 9 to page 344, col. 1, line 6). These cells are not patentably distinguished from the cells claimed. Thus Plump clearly anticipates the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 48, 50, 60, 62 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1997) Science 280, 1256-1258 in view of Arbones et al 1994) Nature Genetics 6, 90-97 and Plump et al (1992) Cell 711, 343-353.

Cibelli teaches the production of transgenic, cloned calves by the production of a bovine fibroblast cells from male fetal tissue, introducing a DNA sequence of interest operably linked to a promoter into the fibroblast cells, and performing nuclear transfer using the transgenic fibroblast cell nucleus as the nuclear donor (page 1256, col. 3, parag. 1, lines 1-14). The nuclear transfer unit is activated and cultured to greater than a 2-cell embryo before transferring into a foster mother (page 1258, col. 2, note 12 to col. 3, line 12). The

transferred embryo develops into a fetus, which develops into a term male calf (page 1257, figure 2). Fetal fibroblasts meant the definition of NENS somatic cells as they are neither embryonic nor sexual tissues. 6.5 day embryos contain more cells than two. The introduction of the DNA sequence into the fibroblast cells is controlled as the procedure is regulated merely by the introduction of the DNA into the fibroblast cells. Cibelli teaches that for gene targeting events by homologous recombination, a type of controlled genetic modification, the selection procedures involved would require more doublings than fibroblasts have prior to senescence (page 1258, col. 3, parag.3, lines 11 to page 1259, col. 1, line 3). Arbones teaches that myoblast cells cultured up to 100 days provide more efficient targeting of non-embryonic cells (page 92, col. 2, parag. 1, line 5 to page 93, line 8). Plump teaches transgenic mice and transgenic mouse embryos whose genome comprises a disruption of in an apo-E gene such that functional apo-E is not produced (page 343, abstract). Plump offers motivation in stating that aterosclerotic lesions had been made. Cibelli offers motivation in stating that the production of bovines my nuclear transfer improves the production of transgenic cattle over traditional transgenic techniques (page 1258, col. 1, parag. 1, lines 14). Thus, it would have been obvious to the ordinary artisan at the time of the instant invention to produce a bovine comprising a disruption in an apo-E gene by nuclear transfer as taught by Cibelli, where the differentiated donor cell had been cultured through 100 doubling as taught by Arbones, and where the differentiated donor cell comprised a disruption apo-E such. The cited prior art provides sufficient teachings, suggestions and motivations for the claimed invention. The determination of experimental protocols, such as the present doubling times, the court has held that "[d]iscovery of optimum value of result effective variable in known process is ordinarily within skill of art (*In re Boesch and Slaney*, 205 USPQ 215 (CCPA 1980).

Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1997) Science 280, 1256-1258 in view of Arbones et al (1994) Nature Genetics 6, 90-97 and Plump et al (1992) Cell 711, 343-353.

Cibelli teaches the production of transgenic, cloned calves by the production of a bovine fibroblast cells from male fetal tissue, introducing a DNA sequence of interest operably linked to a promoter into the fibroblast cells, and performing nuclear transfer using the transgenic fibroblast cell nucleus as the nuclear donor (page 1256, col. 3, parag. 1, lines 1-14). The nuclear transfer unit is activated and cultured to greater than a 2-cell embryo before transferring into a foster mother (page 1258, col. 2, note 12 to col. 3, line 12). The transferred embryo develops into a fetus, which develops into a term male calf (page 1257, figure 2). Fetal fibroblasts meant the definition of NENS somatic cells as they are neither embryonic nor sexual tissues. 6.5 day embryos contain more cells than two. The introduction of the DNA sequence into the fibroblast cells is controlled as the procedure is regulated merely by the introduction of the DNA into the fibroblast cells. Cibelli teaches that for gene targeting events by homologous recombination, a type of controlled genetic modification, the selection procedures involved would require more doublings than fibroblasts have prior to senescence (page 1258, col. 3, parag.3, lines 11 to page 1259, col. 1, line 3). Arbones teaches that myoblast cells cultured up to 100 days provide more efficient targeting of non-embryonic cells (page 92, col. 2, parag. 1, line 5 to page 93, line 8). Plump teaches transgenic mice and transgenic mouse embryos whose genome comprises a disruption of in an apo-E gene such that functional apo-E is not produced (page 343, abstract). Plump offers motivation in stating that aterosclerotic lesions had been made. Cibelli offers motivation in stating that the production of bovines my nuclear transfer improves the production of transgenic cattle over traditional transgenic techniques (page

1258, col. 1, parag. 1, lines 14). Thus, it would have been obvious to the ordinary artisan at the time of the instant invention to produce a bovine comprising a disruption in an apo-E gene by nuclear transfer as taught by Cibelli, where the differentiated donor cell had been cultured through 100 doubling and shown to be efficient as a homologous recombination target as taught by Arbones, and where the differentiated donor cell comprised a disruption apo-E such. The cited prior art provides sufficient teachings, suggestions and motivations for the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

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September 20, 2002